UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,284	11/17/2003	Hashem Akhavan-Tafti	N-1-002	5215

67504 7590 03/10/2010

NEXGEN DIAGNOSTICS, LLC
22900 W. EIGHT MILE ROAD
SOUTHFIELD, MI 48033-4302

EXAMINER	
GROSS, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
03/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

rshandley@beckman.com
dlhetzler@beckman.com
patentadministrationfullerton@beckman.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte HASHEM AKHAVAN-TAFTI, RENUKA DE SILVA,
ROBERT A. EICKHOLT, C. WILLIAM GUNDLACH IV,
RICHARD S. HANDLEY, KENNETH S. LAUWERS,
MARK SANDISON, and WENHUA XIE

Appeal 2009-009746
Application 10/715,284
Technology Center 1600

Decided: March 8, 2010

Before TONI R. SCHEINER, DONALD E. ADAMS, and DEMETRA J. MILLS, *Administrative Patent Judges*.

SCHEINER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the rejection of claims 1, 2, 4, 8, and 11, directed to a solid phase for binding nucleic acids. The claims have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF THE CASE

Claims 1, 2, 4, 8, and 11 are pending and on appeal,[1] and stand rejected under 35 U.S.C. § 103(a) as unpatentable over Hughes[2] and Lough.[3]

Claim 1 is representative of the subject matter on appeal:

1. A solid phase for binding nucleic acids comprising:
a solid support portion comprising a matrix comprising at least one of silica, glass, insoluble synthetic polymers, or insoluble polysaccharides,
a nucleic acid binding portion for attracting and non-covalently and non-sequence specifically binding nucleic acids wherein the nucleic acid binding portion comprises at least one of a ternary sulfonium group, a quaternary ammonium, or a quaternary phosphonium group $PR_3^+ X^-$, and
a cleavable linker portion linking the nucleic acid binding portion to the solid support.

In response to an election of species requirement, Appellants elected a silica matrix solid-support; a C_1-C_{20} alkyl, aralkyl, or aryl quaternary phosphonium salt nucleic acid binding moiety; and a hydrolytically cleavable linker (Appellants' Response of October 3, 2005). It is our understanding that the claims have been examined only to the extent that they read on the elected species.

---

[1] Claims 3, 5-7, 9, 10, and 12-28 are also pending. Claims 3, 6, 7, 13-21, and 24-26 have been withdrawn from consideration. In addition, a rejection of claims 1, 2, 4, 5, 8-12, 22, 23, 27, and 28 under 35 U.S.C. § 112, first paragraph was withdrawn by the Examiner (Ans. 2). Thus, only claims 1, 2, 4, 8, and 11 remain rejected and subject to appeal.

[2] Ian Hughes, *Application of Polymer-Bound Phosphonium Salts as Traceless Supports for Solid Phase Synthesis*, 37 TETRAHEDRON LETTERS 7595-7598 (1996).

[3] US Patent No. 5,900,481, issued May 4, 1999 to Lough et al.

ISSUE

The issue raised by this appeal is whether the Examiner has established that one of ordinary skill in the art would have had a reason to combine Hughes' quaternary phosphonium salts with Lough's linker-functionalized beads in the configuration required by the claims.

FINDINGS OF FACT

FF1 Claim 1 is directed to a solid phase comprising a "solid support portion" (e.g., a bead); a "nucleic acid binding portion;" and a "cleavable linker portion linking the nucleic acid binding portion to the solid support." In keeping with Appellants' election of species, the solid support is a silica matrix; the linker is hydrolytically cleavable; and the nucleic acid binding moiety is an alkyl, aralkyl, or aryl quaternary phosphonium salt.

FF2 Figure 2 of the present Specification is a schematic illustration of the binding and release of a nucleic acid using a solid phase that meets the limitations of claim 1:

FIG. 2

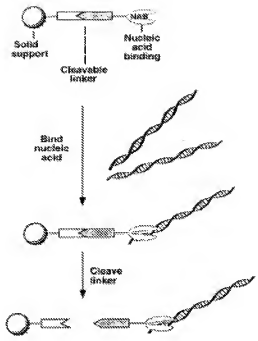

Figure 2 of the Specification shows the structure of a solid phase within the scope of claim 1.

FF3 Hughes teaches that polymer-supported phosphonium salts can be used as "traceless" linkers for solid phase synthesis of combinatorial libraries. A traceless linker is one that "leave[s] no memory" of itself in a synthesized product, once the product is cleaved from the solid phase support. (Hughes 7595, 7597.)

FF4 Lough discloses functionalized beads "conjugated to a solid support and further conjugated to at least one nucleic acid" (Lough, col. 2, ll. 3-4). "As compared to 'flat' surfaces, beads linked to a solid support provide an increased surface area for immobilization of nucleic acids" (*id.* at col. 2, ll. 11-13).

FF5 Lough teaches that "the bead can be comprised of silica gel, glass, [etc.]" (Lough, col. 3, ll. 16-17).

FF6 In a preferred embodiment, "the bead is conjugated to the solid support and/or the nucleic acid is conjugated to the bead using an acid-labile bond. For example . . . a trityl linker" (Lough, col. 5, ll. 6-9).

FF7 Lough also contemplates:

> [T]he use of orthogonally-cleavable linkers for binding the bead to the solid support, and for binding the nucleic acid to the bead. Thus, a bead can be selectively cleaved from the surface without cleaving the nucleic acid from the bead, while the nucleic acid is cleaved from the bead at a later stage. For example, a disulfide linker (which can be cleaved, using, e.g., DTT) could be employed to bind the bead to the solid surface, and a bead-nucleic acid linker involving an acid-cleavable bifunctional trityl group could be used to immobilize a nucleic acid to the bead.

(Lough, col. 5, ll. 18-28.)

FF8 The Examiner finds that "the beaded composition according to Lough et al may be represented as: DNA-linker 1-Bead-linker 2-surface" (Ans. 5).

PRINCIPLES OF LAW

"[T]he Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art." *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992).

> [A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 418 (2007). In other words, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.* (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

ANALYSIS

The Examiner finds that Hughes discloses "hydrolysis of an aralkyl quaternary phosphonim ylide (salt) from a solid matrix" (Ans. 4), but doesn't "teach silica as the solid support . . . [or] binding of nucleic acids" (*id.*). The Examiner further finds that Lough discloses "silica as a support for binding nucleic acids" (*id.*), and also discloses a "Trityl linker" which "falls squarely into the category of cleavable linker portion" (*id.* at 8).

The Examiner concludes that "[o]ne of ordinary skill in the art would have been motivated to make and use the chemistry of Hughes with the silica beads of Lough et al to take advantage of the chemical versatility afforded by orthogonal nucleic acid binding" (Ans. 4).

Appellants contend that the Examiner's "proposed combination results in a material in which one or more elements of the claims are missing" (App. Br. 6), specifically, the combination would not result in "a cleavable linker linking the nucleic acid binding portion to the solid support" (*id.* at 8). We agree.

As discussed above, Lough's reference to "orthogonally-cleavable linkers" refers to a configuration where one cleavable linker is used to bind the bead to the surface, and a different linker, cleavable under different conditions, is used to bind the DNA to the bead (FF7). Thus, "a bead can be selectively cleaved from the surface without cleaving the nucleic acid from the bead, while the nucleic acid is cleaved from the bead at a later stage"

(*id.*). The Examiner found that the configuration of Lough's composition could be represented as:

DNA-linker 1-Bead-linker 2-surface.

(Ans. 5, FF8.) Thus, if we accept for the sake of argument that it would have been obvious to "use the chemistry of Hughes with the silica beads of Lough et al to take advantage of the chemical versatility afforded by orthogonal . . . binding" (Ans. 4), Hughes' phosphonium salt would be linker 1, and Lough's trityl group would be linker 2, the bead would be between the two linkers, and the resultant configuration would be represented as:

DNA-phosphonium salt-Bead-trityl group-surface.

In contrast, the claims require a configuration with the cleavable linker *between* the bead and the phosphonium salt.

In an alternative rationale, the Examiner observes that "the teachings of Lough et al and Hughes may be put together in many ways which read on the claimed subject matter. For example, one of skill in the art might construct DNA^-:::RP^+Ph_2-Optional Spacer-Trt-Bead, with RP^+Ph_2- from Hughes" (Ans. 8).

Nevertheless, while one could conceivably combine the various components of Hughes and Lough to arrive at the structure proposed by the Examiner, we agree with Appellants that the Examiner has offered no reason "why one of skill in the art would be motivated to introduce the extra complication" of a cleavable linker between the bead and the phosphonium salt (Reply Br., section 2).

CONCLUSIONS OF LAW

The Examiner has not established that one of ordinary skill in the art would have had a reason to combine Hughes' quaternary phosphonium salts with Lough's linker-functionalized beads in the configuration required by the claims.

The rejection of claims 1, 2, 4, 8, and 11 under 35 U.S.C. § 103(a) as unpatentable over Hughes and Lough is reversed.

REVERSED

cdc

NEXGEN DIAGNOSTICS, LLC
22900 W. EIGHT MILE ROAD
SOUTHFIELD, MI 48033-4302